

COMPOUNDS AND USES THEREOF

BACKGROUND

[0001] The invention relates to compounds useful for modulating BRG1- or BRM-associated factors (BAF) complexes. In particular, the invention relates to compounds useful for treatment of disorders associated with BAF complex function.

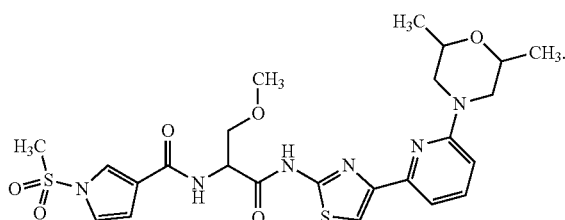
[0002] Chromatin regulation is essential for gene expression, and ATP-dependent chromatin remodeling is a mechanism by which such gene expression occurs. The human Switch/Sucrose Non-Fermentable (SWI/SNF) chromatin remodeling complex, also known as BAF complex, has two SWI2-like ATPases known as BRG1 (Brahma-related gene-1) and BRM (Brahma). The transcription activator BRG1, also known as ATP-dependent chromatin remodeler SMARCA4, is encoded by the SMARCA4 gene on chromosome 19. BRG1 is overexpressed in some cancer tumors and is needed for cancer cell proliferation. BRM, also known as probable global transcription activator SNF2L2 and/or ATP-dependent chromatin remodeler SMARCA2, is encoded by the SMARCA2 gene on chromosome 9 and has been shown to be essential for tumor cell growth in cells characterized by loss of BRG1 function mutations.

[0003] Deactivation of BRG and/or BRM results in downstream effects in cells, including cell cycle arrest and tumor suppression.

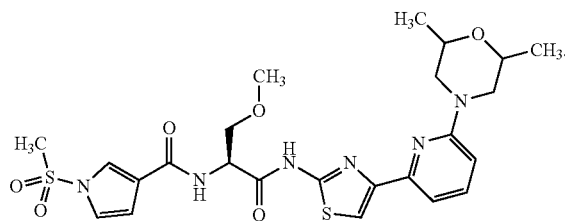
SUMMARY

[0004] The present invention features compounds useful for modulating a BAF complex. In some embodiments, the compounds are useful for the treatment of disorders associated with an alteration in a BAF complex, e.g., a disorder associated with an alteration in one or both of the BRG1 and BRM proteins. The compounds of the invention, alone or in combination with other pharmaceutically active agents, can be used for treating such disorders.

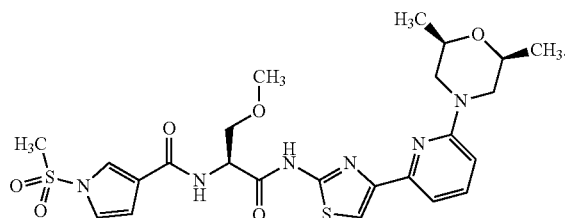
[0005] In an aspect, the invention features a compound, N-(1-((4-(6-(2,6-dimethylmorpholino)pyridin-2-yl)thiazol-2-yl)amino)-3-methoxy-1-oxopropan-2-yl)-1-(methylsulfonyl)-1H-pyrrole-3-carboxamide, or a pharmaceutically acceptable salt thereof, having the structure:



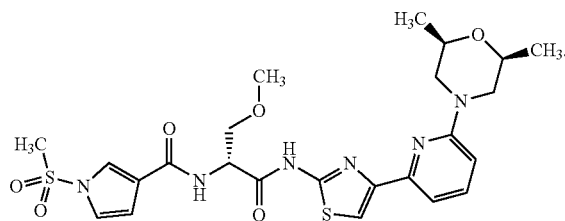
[0006] In some embodiments, the compound, or a pharmaceutically acceptable salt thereof, has the structure:



[0007] In some embodiments, the compound, or a pharmaceutically acceptable salt thereof, has the structure:



[0008] In some embodiments, the compound, or a pharmaceutically acceptable salt thereof, has the structure:



[0009] In another aspect, the invention features a compound, N-(1-((4-(6-(2,6-dimethylmorpholino)pyridin-2-yl)thiazol-2-yl)amino)-3-(methoxy-d3)-1-oxopropan-2-yl)-1-(methylsulfonyl)-1H-pyrrole-3-carboxamide, or a pharmaceutically acceptable salt thereof, having the structure:

